Self-management interventions for pain and physical symptoms among people living with HIV: a systematic review of the evidence

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Conflict of Interest

AW reports personal fees from Advisory boards or speaker fees from GSK, ViiV Healthcare, Gilead Sciences and Janssen, grants from Grants to Imperial College London from Gilead Sciences, ViiV Healthcare, Janssen, BMS and Merck, outside the submitted work.

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Introduction

Evidence shows a substantial decline in mortality among people living with HIV (PLWH) resulting in increased life expectancy [1, 2]. PLWH experience a high burden of pain and physical symptoms. It is hypothesised that PLWH experience pain due to severity of their underlying HIV infection and side effects of HIV treatment [3]. Recent evidence also suggests inflammation as a potential aetiology [4]. A systematic review of pain in HIV/AIDS reported that pain prevalence ranges from 54% (point prevalence) to 83% (three-month period prevalence) [5]. Peripheral neuropathy (PN) is common in HIV infection despite the use of effective ART [6], with a prevalence range of 44%-60% [7-9]. Longitudinal studies conducted in high income countries report that the prevalence of PN is increasing despite the decline in use of neurotoxic drugs [10, 11]. An observational cohort study reported a prevalence of mild PN of 38%. It is often under recognised and, given the increased survival of PLWH, the prevalence of this problem is actually greater than the historically-reported rates of severe PN from studies conducted prior to ART [12]. Pain is considered chronic if it has a duration of at least three months beyond the period of normal healing [13]. Pain in HIV is often undertreated, underreported, and unlikely to be routinely assessed [14].

PLWH also experience a high burden of physical symptoms [15, 16] from diagnosis [17, 18], in advanced disease and while on active ART [15, 19]. Common symptoms include fatigue (61%-72%) [8, 20, 21], headache (31.8%-42%) [7, 22, 23], anorexia (44%-49%), nausea/vomiting (25%-50%), diarrhoea (6%-54%), and weight loss (8%-89%) [8, 17, 18, 22, 24], pruritus/itching (67%) [8, 17], chills, rash (32.8%-50.4%) [22, 23, 25], sweat, fever (32%-89%) [18, 21], dyspnoea (30.8%) [18, 21-23], and cough (53%) [8, 18, 22].

Pain and physical symptoms are associated with poor drug adherence [26, 27], viral load rebound, [19], poor quality of life [28-31], and distress [32-34]. Furthermore, patients in pain are likely to be involved in risky behaviours such as alcohol use, intravenous drug use [5, 22, 35], and sexual risk taking [36]. Pain experience also results in treatment switching

[37, 38], and suicidal ideation [18, 39].

Self-management intervention include activities individuals take for themselves and their families to stay fit and maintain good health [40]. Evidence-based self-management interventions have the potential to help PLWH to successfully monitor pain and physical symptoms [41].

Although there is some evidence from a systematic review that self-management interventions have positive effects in improving physical, psychosocial, knowledge and behavioural outcomes among PLWH [42], this review covered studies conducted until 2010, focused on educational interventions only and excluded studies conducted in Africa. This removes the opportunity for us to learn from effective interventions that may have potential for replication in high income/developed countries (south to north learning). Furthermore, little is known about the effective methods of supporting caregivers in their role in pain and symptom management among PLWH.

We aimed to systematically identify and appraise the evidence regarding the effectiveness of self-management interventions for pain and/or physical symptoms for PLWH and/or their caregivers.

Methods

Search strategy and selection of studies

The full protocol is registered with PROSPERO, number CRD42017055857 [43]. We searched in Amed, Assian, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, Embase, Medline, PsycInfo, Scopus and Web of Science from 1984 (when HIV was first reported) to May, 2018. Key words and subject headings were used (see table 1). Key words/concepts for pain and physical symptoms were based on the Revised Sign and Symptom Check-List for HIV [29], which captures physical symptoms including those related to the impact of HIV treatment [29]. Reference lists of identified papers were hand searched.

Subject headings and word truncations were entered according to requirements of each database to map all possible keywords. HIV was combined with AIDS using the 'OR' function (Group 1). All the interventions were combined using the 'OR' function (Group 2). Pain and symptoms were combined using the 'OR' function (Group 3). Finally search strategies 1, 2 and 3 were intersected using the 'AND' function.

We included studies which recruited PLWH and informal caregivers, any self-management interventions, published randomised/non-randomised trials written in English language, and studies reporting pain and physical symptom outcomes. We excluded studies that recruited patients without HIV diagnosis, and formal caregivers, unpublished studies, and qualitative studies, studies without a comparison group (see table 2).

A PRISMA flow chart (see figure 1) reports the study selection process [44]. All references from the initial database and hand searching were exported to Endnote version 6, and the database was de-duplicated. KN independently evaluated all references by reviewing titles and abstracts according to the inclusion and exclusion criteria. If the title and abstract were clearly irrelevant, the reference was excluded. The full text of retained references was obtained and the content reviewed against the inclusion and exclusion criteria. Any reference for which inclusion and exclusion criteria were unclear was discussed with a second reviewer (RH). Disagreements between the reviewers were resolved through discussion with the review team.

Data extraction

KN extracted data from studies using methods described in the Cochrane handbook for systematic reviews of interventional studies [45]. A standardised data extraction form was used to ensure consistency in the review [46]. The review team checked data extraction based on the standardised form and any queries were resolved through discussion.

Methodological quality of the studies

KN assessed the quality of each study independently using the Joanna Briggs Institute Critical Appraisal checklist for Randomised and non-Randomised trials (see table 7) [47]. RH checked the critical appraisal, and discrepancies in the assessment for quality were resolved through discussion. Table 3 provides summary of quality assessment of each study. GRADE was used to rate the quality of each outcome (table 4) [48].

Many studies did not provide sufficient details to allow a detailed assessment of methodological quality. Nine studies were judged "adequate" on randomisation procedures [49-58], while seven studies did not report methods of randomisation [59-65].

Three studies blinded participants by use of a dummy intervention [50, 51, 59]. In the first study, participants in the intervention wore earphones and listened to tapes with instructions to elicit a relaxation response, while participants in the control group wore earphones and listened to soft music routinely played in the clinic [50]. In the second study, participants in the intervention group attended six educational sessions on diarrhoea management using food, while the control group also attended educational sessions on general self-care and healthy living with HIV [51]. In the third, participants in the intervention arm received a symptom management manual while participants in the control arm received a general nutritional management manual. Both manuals were similar in size [59].

Five studies reported blinding of outcome assessors [52, 56, 58, 63, 64]. Allocation concealment of the person randomising participants was reported in six studies [50, 51, 54-57, 66]. Collection of outcome data differed in these studies; five studies collected data via self-administered questionnaires [49, 59, 60, 64, 67], two studies used online data collection [54, 57, 67], and two studies used postal questionnaires [60, 64]. Seven studies reported attrition rates ranging from 24%-34.6% [50, 51, 54, 57, 59, 66-68].

Intention to treat analysis (ITTA) was only applied in four studies [50, 58, 59, 65]. The remaining studies excluded all participants lost to follow-up. However two studies [49, 55]

did not provide details about losses to follow-up, including methods of handling this in analysis.

Quality of evidence

Quality of evidence was moderate for pain severity, pain interference, and symptoms of diarrhoea and low for physical symptoms, quality of life, and knowledge outcomes. Evidence was very low for symptoms of fatigue and weight loss/gain. All these outcomes are patient reported and were downgraded due to serious risk of bias from lack of blinding and insufficient details about randomisation methods, and attrition. Quality of evidence was further downgraded because of serious inconsistency due to heterogeneity of the participants, interventions and use of tools without established psychometric properties.

Findings

Characteristics of the studies

A total of 22 papers, reporting 19 different studies, met the inclusion criteria (three studies were reported in two papers each). Tables 5 and 6 presents detailed data on each study. The total number of participants was n=2189 patients and n= 218 caregivers. The majority of studies were conducted in high-income countries (n=15), predominantly in the USA.

Of the 19 studies, 17 were RCTs and two used quasi-experimental designs [67, 68]. Sample size ranged from 27 [58] to 775 [59]. Two RCTs recruited both patients and family caregivers [56, 64]. Most studies allocated participants to one of the two arms, but three studies randomised to three arms [49, 61, 64, 69].

The interventions included face-to-face sessions (15-90 minutes) combined with information leaflet/booklet and work book for participants to take away with them [55, 56, 58, 59, 63, 65]. Two studies delivered an intervention online [54, 57, 67]. Three studies used cell phones or phone call to provide the intervention exclusively [53] or as a reinforcement [56, 69].

Nine studies were delivered by health care professionals [51, 52, 56, 67], while four were delivered by peer-leaders [54, 58, 60, 65]. None of the studies reported data on cost effectiveness of the interventions. Duration of follow-up varied from three weeks [51] to 24 weeks [51].

Pain and physical symptom outcomes

Three studies reported data on pain severity as a primary outcome, and two studies reported data on pain interference as a secondary outcome. Only one study found significant differences on pain severity and interference [56]. Nkhoma et al (2015) used the Brief Pain Inventory and found significant differences on pain severity and pain interference between a nurse-led pain educational intervention (consisting of an information leaflet, face-to-face discussion and a phone call) and usual care [56]. Nkhoma et al (2015) trial was a one-off intervention and follow-up was at eight weeks. Parker et al (2016) used the BPI-Xhosa and found no significant differences between a peer-led exercise and education intervention and usual care on pain severity and interference [58]. Parker et al (2016) trial consisted of two-hourly sessions and workbook on self-management of pain and physical symptoms for six weeks. Questionnaires were administered monthly for four months. Gifford et al (1998) assessed pain with the Medical Outcomes Study and found no significant difference between a peer-led positive self-management programme (PSMP) intervention and usual care [60]. The intervention consisted of seven interactive health education group sessions on self-management skills and information on symptom assessment and management, medication use, physical exercise, relaxation, communication with doctor and nutrition. Participants were followed-up at three months. Although the quality of evidence in studies that assessed pain outcomes was downgraded due to risk of bias following lack of blinding, the overall quality of evidence was moderate.

Symptom severity and frequency was reported in eight studies [53, 54, 59, 60, 62, 64, 65, 67]. Three of the eight studies reported significant decrease in symptom severity [53, 59, 60] and frequency [53, 59]. Vidrine et al (2007) used the HIV related symptom status

and reported a significant decline in symptom frequency and burden among the intervention group compared to the control group [53].

Wantland et al (2008) used a revised sign and symptom checklist to evaluate symptom frequency and intensity and reported a significant decrease in symptom frequency and intensity among the symptom management manual group compared to the nutritional management manual group [59]. In a positive self-management programme (PSMP), Gifford et al (1998) created their own instrument to assess symptom severity and reported significant improvement in the intervention group compared to the control group [60].

However Webel (2010) who randomised HIV positive women to receive a positive self-management programme (PSMP) developed by Gifford et al (1998) or HIV symptom management manual developed by Wantland et al (2008) failed to demonstrate effectiveness of the intervention [65]. Likewise Inouye et al (2000) reported non-significant results between the self-management training and education programme intervention and usual care [62]. A positive outlook peer-led online-self management intervention among gay men reported nonsignificant results on physical health and symptoms [54, 57]. Pakenham et al (2002) used the brief symptom inventory and reported a non-significant decrease in symptom distress between two intervention groups and the control group [64]. A non-randomised online self-management intervention study assessed symptoms with the HIV symptom index, but did not observe significant differences between the self-management skills sessions and traditional care [67].

Symptoms of fatigue were examined in two studies [49, 60], with one study reporting that the guided imagery intervention showed a significant decrease in fatigue compared to the relaxation response intervention and usual care [49].

Symptoms of weight loss and gain were examined in two studies which evaluated effect of self-management dietary interventions on weight [55, 68]. One study was interested in weight loss [55], while another was interested in weight gain [68]. Both studies showed significant effects of a diet programme on weight.

Symptoms of diarrhoea were reported in one study. This was a nurse-led dietary intervention. Participants were instructed to eat a low fat, lactose free, low insoluble fiber, high soluble fiber, and caffeine-free diet, including preparation of tasty foods in line with the diet, strategies to keep the diet cost-efficient. Comparison group were provided with standard information on safe-care and healthy living with HIV-AIDS, without information about diet, and received the intervention after completion of the study. Both groups attended six study sessions, with measurers administered at three and 24 weeks. The intervention group reported significant improvement in stool frequency and consistency at three weeks and 24 weeks [51].

Symptoms of oral candidiasis were reported in one study. A dentist delivered intervention reported that oral hygiene and instructions showed non-significant effects on recurrence of oral candidiasis, self-diagnosis, prevalence of candidiasis [63].

Sleep duration and quality was reported in one study [52]. A nurse and health educator delivered the intervention on management of HIV and sleep related problems. The study reported non-significant effects on sleep duration, sleep efficiency, sleep fragmentation, disturbances and sleep impairments.

Quality of life and knowledge outcomes

Quality of life was reported in nine studies [52, 54, 56, 57, 62, 64-66, 69]. Four studies reported statistically significant effects of the intervention on some subscales of quality of life [56, 57, 64, 69]. Knowledge outcomes were reported in six studies [54, 56, 57, 60, 61, 64], with four studies reporting statistically significant effects [56, 57, 61, 64] while two reported no effects [54, 60].

Outcomes for caregiver participants

Two studies randomised both patients and caregivers. One was conducted in Malawi [56] and another one in Australia [64]. The Malawian study was a two arm trial (details provided on pain severity and interference outcomes), while the Australian study was a three arm trial. In the Australian study, caregivers in arm 1 received the intervention

with their patients, caregivers in arm 2 received the intervention, but not their patients, and caregivers in arm 3 received standard care. The intervention consisted of eight weekly sessions of one and half hours conducted by psychologists. Based on two HIV target problems which participants stated.

Both studies reported significant improvement in knowledge and quality of life outcomes [56, 64]. Furthermore, Nkhoma et al (2015) reported significant improvement in caregiver motivation to provide care. Pakenham et al [50] reported data on caregiver global distress. Caregivers who received the intervention with their patients (arm1), experienced significant improvements in global distress compared to caregivers who received the intervention alone (arm2) and caregivers who received standard care (arm3). However, social adjustment did not differ significantly between the three groups.

Discussion

Despite the clinical burden of pain and physical symptoms among PLWH, this systematic review identified only three studies that examined the effects of self-management interventions on pain outcomes and eight studies on physical symptom outcomes. Most of the studies reviewed were of low quality due to risk of bias and inadequate reporting [49, 53, 55, 59, 62, 65, 67, 68, 70]. Most of the included studies were conducted ten years ago [49, 51, 53, 59, 61-66, 68-70] and predominantly in the USA [49, 51, 53, 59, 62, 63, 65, 70].

Two studies with positive outcomes delivered the intervention once [56, 59], however in most of the studies [49, 53, 55, 61, 64, 66, 69] participants had multiple exposure to the intervention. We therefore can say that both one off intervention and ongoing sessions were effective. Studies with positive results had short-term follow-up (six and 12 weeks) [53, 55, 57, 59, 61, 64, 66, 69] including one study which conducted follow-ups at 24 weeks [51]. Some studies conducted a one off follow-up assessment [49, 53, 55, 56, 61,

69]. It is therefore difficult to infer if the positive benefits observed could be sustained over time. Some studies conducted multiple follow-ups [51, 57, 59, 66]. In Wantland et al,(2008) study, symptom prevalence significantly declined at week four with a further significant decline at week 12 [59] . Likewise, Anastasi et al, (2006) study, the intervention showed significant improvement at week three and this was further significant at week 24 [51]. However, in Millard et al; 2016 study, some quality of life sub-scales (emotional distress) were significant at week eight, but not significant at week 12. Body change and social relationships were not significant at week eight, but were significant at week 12. In the same study, the intervention showed significant improvements in constructive attitudes and approaches, skill and technique acquisition, and health service navigation at week eight, but these were not significant at week 12. Furthermore, the intervention group improved significantly on self-management skills: Positive outlook self-efficacy subscales (relationships, social participation and emotions) at week 8, but these were not significant at week 12.

We therefore can say that in some studies positive outcomes were sustained over time, while in some studies they were not sustained. Furthermore, in some studies it is difficult to know because they conducted one-off follow-up assessment.

Among caregiver participants, only two studies reported data on caregiver outcomes with both studies reporting statistically significant results across most outcomes.

There is some evidence to suggest that self-management interventions delivered either online/computer-based, face-to-face discussion or group-based including booklet, leaflet or manuals are effective in improving pain, physical symptoms quality of life and knowledge. These results are in line with findings from systematic review of person-centred pain management educational interventions in cancer population [71, 72].

Based on these findings, there is limited evidence that self-management interventions among HIV-infected individuals with chronic pain and high burden of physical symptoms are effective.

Interestingly studies which used cheap and locally available resources (such as food locally available to self-manage diarrhoea, or information leaflets) [51, 55, 68] were effective compared to some technology based interventions such as computer sessions [54, 67]. Although some self-management interventions were not effective, but they helped to promote health behaviours such as modification of food habits by reducing sugar meals thereby preventing dental caries [63], likewise physical exercises meant to reduce symptoms but do help in reducing weight and preventing cardiovascular conditions [60].

There is a very well established self-management literature of chronic diseases such as diabetes [73], as well as self-management of pain, physical and emotional functions, and quality of life among patients with chronic back and musculoskeletal pain and various disease conditions [74-78]. Self-management is useful in other populations and for other outcomes, but there is little high quality research on the topic in HIV population. Self-management of pain and symptoms in PLWH is still a new field with lots of work to be done.

Behavioural change was the main focus of the theoretical approaches used in the studies reviewed. Banduras self-efficacy theory [79] was frequently used with an underlying premise that patients' belief in their own ability to accomplish a specific health behaviour or achieve a reduction in pain or symptom severity and frequency leads to improved health outcomes [80, 81].

This review provides a better understanding of the state of science and potential areas for future research on the effectiveness of self-management interventions for PLWH and their caregivers. Future research areas include self-management interventions using theoretically plausible models for adults with HIV/AIDS and self-management interventions for adolescents with HIV/AIDS. There is a need to conduct well-designed multi-centre and national trials to evaluate their effectiveness since evidence from these studies reviewed mostly focused on one region with few study sites.

This is the first review of self-management interventions in HIV population to include studies conducted across the globe, focussing on different models of self-management and targeting patients and their informal caregivers.

Studies reviewed were not adequately explicit about methods in order to judge the quality of evidence. Sample size was very small in most of the studies reviewed and a high attrition rate was also common in these studies. There was a great degree of heterogeneity in the studies therefore it was inappropriate to pool data due to differences in nature and context of the interventions, instruments used, duration of the interventions and period of follow-up.

The review has identified interventions with potential and gaps in evaluation methods for self-management interventions in HIV/AIDS population.

Conclusions

Given the high prevalence and burden of pain and physical symptoms among PLWH, and the clinical and public health implications of this, relatively few studies and fewer recent ones [52, 54, 56-58, 67] were identified in this review. Only three studies assessed pain as an outcome, and one of these reported significant results. The included studies differed largely in several aspects including clinical settings, outcome measures and assessors, type of the intervention, duration of the study and type of symptoms.

There is some evidence to suggest that self-management interventions delivered either online, face-to-face or group-based consisting of booklet, leaflet or manuals are effective in improving pain and physical symptoms. However caution is needed when interpreting these studies because the quality of evidence is relatively poor due to methodological weaknesses of some designs related to small sample sizes [58, 62-64, 70], high attrition rate [50, 51, 54, 59, 66-68], and use of instruments without established psychometric properties [54, 57, 60]. We recommend modelling a theoretically plausible, feasible and

acceptable intervention for pain and symptom self-management among culturally diverse people with HIV using an RCT design.

Authors contributions

All authors contributed to and approved the systematic review protocol. KN conducted the search. KN and RH extracted data, assessed risk of bias and graded the evidence. CN verified data extraction where necessary. All authors then reviewed data extraction and contributed to interpretation. KN drafted the manuscript. All authors reviewed the manuscript and each made a significant contribution to successive drafts. All authors approved the manuscript.

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